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Renal Involvement in Systemic Diseases: A 13-Year Retrospective Renal Biopsy Study in Sub-Saharan African Patients

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Abstract

Background: Renal involvement is a frequent and potentially severe complication of systemic diseases, particularly immune-mediated disorders. Renal biopsy remains the gold standard for diagnosing, classifying, and guiding the management of renal lesions associated with these conditions. Data from Sub-Saharan Africa remain limited. **Objectives:** To describe the clinical indications and histopathological spectrum of renal involvement in systemic diseases based on renal biopsy findings over a 13-year period in a tertiary referral center in Sub-Saharan Africa. **Methods:** We conducted a single-center retrospective observational study from January 2011 to December 2023 in a university hospital pathology center in Senegal. All patients with a known or suspected systemic disease who underwent a renal biopsy and had histologically confirmed renal involvement were included. Sociodemographic data, biopsy indications, and histopathological findings were analyzed descriptively. **Results:** A total of 263 patients were included, representing 7.95% of all renal biopsies performed during the study period. The mean age was 39.1 ± 12.6 years, with a female predominance (72%). Renal biopsy indications were mainly related to systemic lupus erythematosus (SLE) (65.39%), dominated by proteinuria and renal failure. In 43.34% of cases, the diagnosis of the systemic disease was established based on renal biopsy findings. Histopathologically, membranous glomerulopathy and lupus nephritis were the most frequent lesions, with a predominance of proliferative forms, particularly class IV (22.05%) and class III (11.02%). Other lesions included membranoproliferative glomerulonephritis,

crescentic glomerulonephritis, amyloidosis, tubulointerstitial nephritis, and thrombotic microangiopathy. SLE was the most common underlying systemic disease (80.60%), followed by cryoglobulinemia and amyloidosis among non-autoimmune conditions. **Conclusion:** Renal involvement in systemic diseases exhibits a wide clinical and histological spectrum, largely dominated by lupus nephritis. Given the nonspecific clinical presentations, renal biopsy is essential for accurate diagnosis, prognostic assessment, and therapeutic decision-making. These findings highlight the importance of improving access to renal biopsy and conducting prospective studies in Sub-Saharan Africa.

Keywords

Systemic Lupus Erythematosus, Sub-Saharan Africa, Renal Biopsy

1. Introduction

Renal involvement is a major and potentially severe complication of systemic diseases, particularly immune-mediated disorders. Glomerulonephritis represents a heterogeneous group of renal diseases resulting from immune and inflammatory mechanisms that may lead to chronic kidney disease or end-stage renal disease (ESRD) [1]. Renal biopsy remains the gold standard for the diagnosis and classification of glomerular diseases associated with systemic disorders and plays a central role in therapeutic decision-making and prognostic assessment [2].

Systemic lupus erythematosus (SLE) is the systemic disease most frequently associated with renal involvement. Lupus nephritis affects a substantial proportion of patients and represents a major determinant of morbidity and long-term renal outcome [3]. Its histological spectrum is broad, ranging from mild mesangial lesions to severe proliferative and membranous forms, which are associated with a higher risk of renal function decline [4]. Despite advances in immunosuppressive therapy, lupus nephritis continues to be associated with a significant risk of progression to ESRD [5].

Beyond SLE, other systemic diseases such as systemic vasculitides and connective tissue disorders may also cause diverse patterns of renal involvement, underscoring the heterogeneity of renal lesions in systemic diseases. In this context, renal biopsy remains essential to accurately characterize renal lesions and guide optimal management.

The objectives of this study were to describe the clinical indications and histopathological spectrum of renal involvement in systemic diseases based on renal biopsy findings over a 13-year period in a tertiary referral center in Sub-Saharan Africa.

2. Patients and Method

2.1. Study Design and Setting

This was a single-center, retrospective observational study conducted in a refer-

ence university hospital pathology (anatomopathology) center in Senegal, involving close collaboration between the nephrology department and the pathology department.

The center receives patients referred for diagnostic evaluation of renal involvement in the context of systemic diseases, originating from various clinical departments (nephrology, internal medicine, rheumatology).

2.2. Study Period

The study was carried out over a thirteen (13)-year period, from January 2011 to December 2023, and included all renal biopsies performed during this time.

2.3. Study Population

2.3.1. Inclusion Criteria

The study included:

- patients with a known systemic disease who underwent a renal biopsy;
- patients in whom a systemic disease was identified or suspected based on the histopathological findings of the renal biopsy.

2.3.2. Non-Inclusion Criteria

The following were excluded:

- patients with diabetes mellitus or systemic infectious diseases, in order to avoid bias related to metabolic or infectious causes of kidney disease;
- patients with a systemic disease who did not undergo a renal biopsy; inadequate, non-diagnostic, or insufficient renal biopsies (insufficient number of glomeruli or unusable material).

2.4. Sampling Method

An exhaustive sampling strategy was used, including all patients meeting the inclusion criteria throughout the entire study period, without prior calculation of sample size.

2.5. Data Collection

Data were collected retrospectively from:

- the pathology department registers;
- histopathological reports of renal biopsies;
- clinical medical records, when available;
- Data were recorded on a pre-established standardized data collection form to ensure uniformity.

2.6. Variables Studied

2.6.1. Sociodemographic Variables

- age at the time of renal biopsy;
- sex.

2.6.2. Definition of Study Variables

Nephrotic syndrome was classified as impure when associated with at least one of the following criteria: hematuria defined by the presence of more than five red blood cells per high-power field on urine sediment examination, arterial hypertension defined as blood pressure values greater than or equal to 140/90 mmHg, and/or renal insufficiency defined by an estimated glomerular filtration rate below 60 mL/min/1.73m^2.

2.6.3. Histopathological Variables

- type of renal involvement (glomerular, tubulointerstitial, vascular);
- specific type of glomerular lesion;
- presence of activity and/or chronicity lesions;
- classification of lupus nephritis according to the ISN/RPS classification, when applicable [4];
- type of amyloidosis (AA, AL) when identified.

2.7. Histopathological Methods

A renal biopsy specimen was considered adequate when it contained at least 8 evaluable glomeruli on light microscopy. Samples not meeting this minimum requirement were excluded from the analysis. Renal biopsies were analyzed by light microscopy after standard staining procedures (hematoxylin-eosin-saffron, PAS, Masson's trichrome, and silver staining when available).

Direct immunofluorescence was performed when tissue was available, allowing detection of immunoglobulin deposits (IgG, IgA, IgM) and complement fractions (C3, C1q).

Electron microscopy was not routinely available and was therefore not included in the standard analysis.

2.8. Statistical Analysis

Data were collected using a pre-established form and entered with Sphinx software version 5.1.0.2. Data analysis was performed using SPSS (Statistical Package for the Social Sciences) version 21. Descriptive analysis included calculation of frequencies and proportions for qualitative variables, and means and standard deviations for quantitative variables.

3. Results

During the study period from 2011 to 2023, a total of 263 patients with a systemic disease associated with histologically confirmed renal involvement were included.

These cases accounted for 7.95% of all renal biopsies performed during the study period (**Figure 1**). The study population showed a predominance in the 30 - 39-year age group.

The mean age was 39.1 ± 12.6 years, with a range from 13 to 70 years. A female predominance was observed, with 72% women (n = 209) and 28% men (n = 54), corresponding to a male-to-female sex ratio of 0.26.

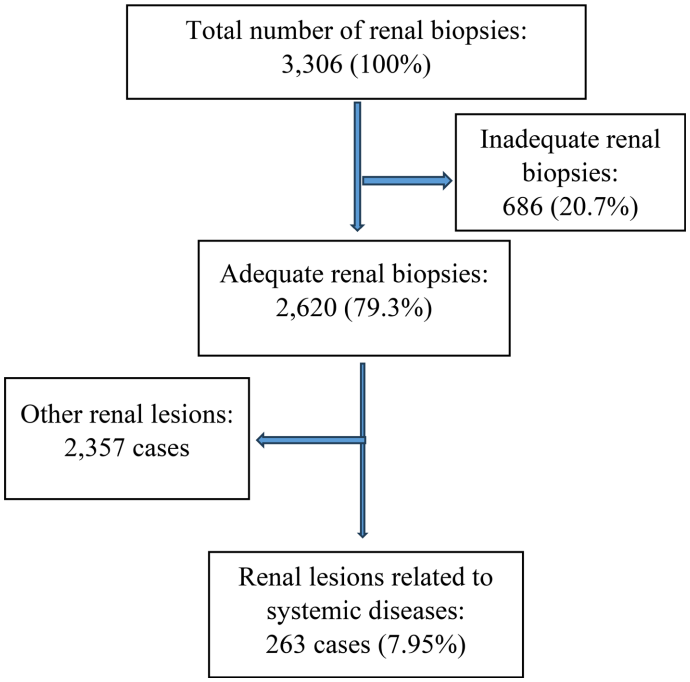

Figure 1. Diagramme de flux.

3.1. Indications for Renal Biopsy

The main indications for renal biopsy were dominated by renal involvement occurring in the context of SLE, accounting for 65.39% of cases (Table 1).

These indications were distributed as follows: proteinuria in SLE (37.64%), renal failure in SLE (18.63%) and impure nephrotic syndrome in SLE (9.12%). Isolated impure nephrotic syndrome accounted for 18.25% of indications (n = 48). In 43.34% of cases, the diagnosis of the systemic disease was established on the basis of the renal biopsy findings.

3.2. Histopathological Diagnosis

Acute glomerular forms: Acute glomerular lesions were infrequent. Crescentic glomerulonephritis was identified in 9 patients (3.42%).

Chronic glomerular forms: Chronic glomerular involvement was dominated by lupus nephritis. The distribution of histological classes showed a predominance of membranous glomerulopathy (22.81%), class IV lupus nephritis (22.05%) and class III lupus nephritis (11.02%). Among the 60 patients with membranous nephropathy (MN), 57 had class V lupus nephritis.

Acute interstitial forms: Acute interstitial lesions were mainly represented by acute interstitial nephritis, observed in 3 patients (1.14%).

Chronic tubulointerstitial forms: Chronic tubulointerstitial nephritis was identified in 4 patients, representing 1.52% of cases.

Acute vascular forms: Acute vascular lesions were mainly represented by thrombotic microangiopathy, observed in 7 patients (2.64%). Three cases of nephroangiosclerosis were also identified (Table 2).

Table 1. Indications for renal biopsy (n = 263).

Indication for renal biopsy	Number of cases	Percentage (%)
Proteinuria in SLE	99	37.64
Renal failure in SLE	49	18.63
Impure nephrotic syndrome	48	18.25
Isolated nephrotic syndrome in SLE	24	9.12
Isolated proteinuria	19	7.22
Proteinuria in rheumatoid arthritis	8	3.04
Renal failure in systemic sclerosis	3	1.14
Renal failure in mixed connective tissue disease	3	1.14
Renal failure in ANCA-associated vasculitis	2	0.76
Renal failure in Multiple myeloma	2	0.76
Proteinuria in autoimmune thyroiditis	1	0.38
Renal failure in dermatomyositis	1	0.38
Proteinuria in IgA vasculitis	1	0.38
Proteinuria in sarcoidosis	1	0.38
Proteinuria in Sjögren's syndrome	1	0.38
Renal failure in multiple autoimmune syndrome	1	0.38
Total	263	100

Table 2. Histological lesions.

Histological lesions	Number of cases	Percentage (%)
Lupus nephritis class IV	58	22.05
Lupus nephritis class III	29	11.02
Lupus nephritis class III + V	29	11.02
Lupus nephritis class II + V	19	7.22
Lupus nephritis class II	1	0.38
Lupus nephritis class IV + V	18	6.84
Membranous nephropathy	60	22.81
Focal segmental glomerulosclerosis	4	1.52
Amyloidosis	13	4.94
Minimal change disease	4	1.52
Membranoproliferative glomerulonephritis (MPGN)	5	1.90
Crescentic glomerulonephritis	9	3.42
Acute interstitial nephritis (AIN)	3	1.14
Chronic tubulointerstitial nephritis	4	1.52
Thrombotic microangiopathy (TMA)	7	2.64
Nephroangiosclerosis	3	1.14

3.3. Distribution of Systemic Diseases According to Histological Diagnosis

Among autoimmune systemic diseases, SLE was the most frequently observed (80.60%), followed by rheumatoid arthritis (3.42%) and systemic sclerosis (1.14%).

Other rarer conditions were also observed, including Sjögren's syndrome (0.38%). Among non-autoimmune systemic diseases, cryoglobulinemia was the most common (4.56%), followed by amyloidosis (3.80%) (Table 3 and Table 4).

Table 3. Distribution of systemic diseases (n = 263).

Systemic disease	Number of cases (n = 263)	Percentage (%)
Autoimmune systemic diseases		
Systemic lupus erythematosus	212	80.60
Rheumatoid arthritis	9	3.42
Systemic sclerosis	3	1.14
Non-specific vasculitis	2	0.76
ANCA-associated vasculitis	2	0.76
Antiphospholipid syndrome	2	0.76
Mixed connective tissue disease	2	0.76
Dermatomyositis	1	0.38
IgA vasculitis (Henoch-Schönlein purpura)	1	0.38
Autoimmune thyroiditis	1	0.38
Multiple autoimmune syndrome	1	0.38
Overlap syndrome	1	0.38
Sjögren's syndrome	1	0.38
Non-autoimmune systemic diseases		
Cryoglobulinemia	12	4.56
Amyloidosis	10	3.80
Randall syndrome	2	0.76
Sarcoidosis	1	0.38

Table 4. Distribution of renal involvement in systemic diseases (n = 263).

Systemic disease	n (%)	Lupus nephritis (classes II; III; IV; V)	Other glomerulonephritis	Amyloidosis (AA/AL)	Tubulointersti tial lesions	Vascular lesions
Systemic lupus erythematosus	212 (80.6)	212 (classes II; III; IV; V; mixed forms)	4 FSGS	-	-	-
Cryoglobulinemia	12 (4.6)	-	5 MPGN	-	-	7 TMA
Rheumatoid arthritis	9 (3.4)	-	4 Crescentic GN	2 AA	3 AIN	-

Continued

Mixed connective tissue disease	2 (0.8)	-	1 MN; 1 Crescentic GN	-	2 Chronic TIN	-
Systemic sclerosis	3 (1.1)	-	1 Minimal change disease	-	1 Chronic TIN	2 TMA
Dermatomyositis	1 (0.4)	-	1 Minimal change disease	-	-	-
ANCA-associated vasculitis	2 (0.8)	-	2 Crescentic GN	-	-	-
Small-vessel vasculitis	2 (0.8)	-	2 Crescentic GN	-	-	-
Autoimmune thyroiditis	1 (0.4)	-	1 MN	-	-	-
Sjögren's syndrome	1 (0.4)	-	1 Minimal change disease	-	-	-
Antiphospholipid syndrome	2 (0.8)	-	-	-	-	2 TMA
Amyloidosis	10 (3.8)	-	-	2 AA; 1 AL; 7 untyped	-	-
Randall disease	2 (0.8)	-	2 Randall-type GN	-	-	-
IgA vasculitis	1 (0.4)	-	-	1 AA	-	-
Sarcoidosis	1 (0.4)	-	-	-	1 Chronic TIN	-
Multiple autoimmune syndrome	1 (0.4)	-	1 Minimal change disease	-	-	3 Nephroangiosclerosis
Overlap syndrome	1 (0.4)	-	1 MN	-	-	-

FSGS: focal segmental glomerulosclerosis; MN: membranous nephropathy; MPGN: membranoproliferative glomerulonephritis; Crescentic GN: crescentic glomerulonephritis; AIN: acute interstitial nephritis; Chronic TIN: chronic tubulointerstitial nephritis; IF: interstitial fibrosis; TMA: thrombotic microangiopathy; NASM/NASB: malignant/benign nephroangiosclerosis.

4. Discussion

In our study, the indications for renal biopsy illustrate the wide spectrum of clinical presentations of renal involvement in systemic diseases, with a clear predominance of situations related to systemic SLE. These findings confirm the central role of renal biopsy in etiological diagnosis, prognostic assessment, and therapeutic decision-making in these complex conditions [1].

4.1. Indications for Renal Biopsy in SLE

Indications related to SLE accounted for more than half of the renal biopsies performed, mainly driven by proteinuria in SLE (37.64%) and renal failure in SLE (18.63%). This distribution is consistent with international recommendations, which advocate performing a renal biopsy in the presence of any significant proteinuria (≥500 mg/24h), with or without impaired renal function, in order to clas-

sify lupus nephritis and tailor immunosuppressive therapy [2] [3].

The high proportion of renal biopsies performed for impure nephrotic syndrome, either isolated or associated with SLE (27.37% overall), reflects the frequency of severe clinical forms in our cohort. These presentations are often associated with proliferative or membranous forms of lupus nephritis, which are known to carry a poor renal prognosis in the absence of early and appropriate treatment [4]. Renal biopsy therefore remains essential to differentiate histological classes, assess activity and chronicity indices, and guide therapeutic strategy [5].

4.2. Indications Outside Lupus: The Key Diagnostic Role of Renal Biopsy

Outside the context of SLE, renal biopsy was mainly indicated for isolated proteinuria (7.22%) or renal failure occurring in other systemic diseases such as rheumatoid arthritis, systemic sclerosis, mixed connective tissue disease, and ANCA-associated vasculitis. In these settings, clinical presentation is often nonspecific and does not reliably predict the underlying type of renal lesion [6].

Indications for renal biopsy due to renal failure in systemic sclerosis, mixed connective tissue disease, and ANCA-associated vasculitis, although numerically limited, represent situations with major prognostic implications. In these diseases, biopsy helps distinguish active glomerular involvement, vascular lesions (notably thrombotic microangiopathy), or tubulointerstitial involvement, each of which is associated with different therapeutic approaches and prognoses [7] [8].

4.3. Isolated Proteinuria and Rarer Indications

Performing a renal biopsy in the presence of isolated proteinuria, whether occurring in a known systemic disease or as the presenting manifestation, highlights the importance of early detection of renal involvement. In conditions such as Sjögren's syndrome, sarcoidosis, or autoimmune thyroiditis, proteinuria may be the sole manifestation of early renal disease, fully justifying the use of renal biopsy [9].

Rarer indications, particularly in multiple myeloma, dermatomyositis, or multiple autoimmune syndrome, emphasize that systemic renal involvement can present with diverse and sometimes atypical clinical patterns. In these situations, renal biopsy enables identification of specific lesions such as amyloidosis, Randall disease, or tubulointerstitial nephropathies, which directly determine therapeutic management [10].

In this study, we analyzed the different forms of renal involvement associated with systemic diseases, highlighting a wide spectrum of lesions affecting the glomerular, tubulointerstitial, and vascular compartments. This heterogeneity reflects the multiplicity of pathophysiological mechanisms involved in these conditions, including immune complex deposition, chronic inflammation, vascular injury, and drug-related toxicity [1].

4.4. Predominance of SLE

SLE was the main etiology, accounting for 80.60% of cases. This predominance is consistent with data from the literature, which identify SLE as the systemic disease most frequently complicated by renal involvement [3] [11].

All patients with SLE had lupus glomerulonephritis, predominantly proliferative classes (II, III, IV), and V. These histological forms are recognized as being associated with a high risk of progression to chronic kidney disease and increased morbidity [4]. Histological classification therefore remains a cornerstone of management, determining both therapeutic strategy and renal prognosis.

The identification of AA amyloidosis in some patients with rheumatoid arthritis suggests prolonged and insufficiently controlled chronic inflammation. Although this association is uncommon, it has been reported in long-standing or severe forms of evolving lupus [12].

4.5. Glomerular Involvement Outside Lupus

Outside SLE, the observed glomerular lesions were mainly crescentic glomerulonephritis, membranoproliferative glomerulonephritis, membranous nephropathy, and minimal change disease.

Systemic vasculitis's, particularly ANCA-associated vasculitis, were mainly associated with crescentic glomerulonephritis. This finding is consistent with histopathological data in the literature, which emphasize the aggressive nature of these lesions, responsible for rapid loss of nephron mass in the absence of early immunosuppressive treatment [7].

Cryoglobulinemia was predominantly associated with membranoproliferative glomerulonephritis, reflecting the role of circulating immune complex deposition and complement activation in the pathogenesis of renal involvement. This association is classically described and well documented in large international series [13].

4.6. Tubulointerstitial Involvement: A Major Prognostic Factor

Tubulointerstitial lesions, particularly acute interstitial nephritis and chronic tubulointerstitial nephropathy, were observed in several systemic diseases such as rheumatoid arthritis, systemic sclerosis, mixed connective tissue disease, and sarcoidosis. These lesions may be related either to the inflammatory activity of the systemic disease itself or to drug toxicity, notably nonsteroidal anti-inflammatory drugs and certain immunomodulatory therapies [14]. Their prognostic significance is major, as tubulointerstitial damage is recognized as a key determinant of kidney disease progression, independently of the associated glomerular lesion type [15].

4.7. Vascular Lesions and Thrombotic Microangiopathy

Vascular lesions, predominantly thrombotic microangiopathy, were particularly observed in antiphospholipid syndrome, systemic sclerosis, and certain vasculitis.

These lesions are known for their severity and their association with rapid progression to advanced or end-stage chronic kidney disease. The presence of benign or malignant nephroangiosclerosis in some cases also suggests the impact of associated factors, particularly chronic hypertension and persistent systemic inflammation, contributing to a worse renal prognosis [16].

4.8. Amyloidosis and Systemic Diseases

Renal amyloidosis was mainly observed in chronic inflammatory diseases, particularly rheumatoid arthritis and lupus. This finding confirms the central role of prolonged inflammation in the pathogenesis of AA amyloidosis [12].

Cases of AL amyloidosis and Randall disease observed in patients with multiple myeloma highlight the need for a rigorous etiological diagnostic approach in any case of renal amyloidosis, in order to adapt therapeutic management appropriately [17].

The exclusion of patients with diabetes mellitus and chronic systemic infectious diseases (HIV, hepatitis B and C, malaria) limits the generalizability of our findings. These conditions represent a substantial proportion of secondary renal diseases in Sub-Saharan Africa. Their exclusion narrows the spectrum of systemic diseases analyzed and may underestimate etiologies that are highly prevalent in our regional context.

The marked predominance of systemic lupus erythematosus (80.60%) in our cohort strongly influences the overall study findings. Therefore, conclusions regarding renal involvement in systemic diseases are largely driven by lupus nephritis data, with limited representation of other connective tissue diseases, vasculitides, or rare autoimmune disorders.

5. Conclusions

This study highlights the wide spectrum of renal involvement in systemic diseases, largely dominated by SLE. Given the often-nonspecific clinical presentation, renal biopsy remains essential for accurate diagnosis, prognostic assessment, and therapeutic guidance. The predominance of proliferative lupus nephritis underscores the potential severity of renal involvement and the importance of early diagnosis.

These findings emphasize the need to strengthen access to renal biopsy and to promote prospective studies in African settings.

6. Limitations

This study has several limitations that should be acknowledged.

First, the retrospective and single-center design may have introduced selection bias and limits the ability to establish causal relationships between systemic diseases and renal involvement. In addition, data collection relied on available medical records and pathology reports, which may have resulted in incomplete clinical information for some patients.

Second, the marked predominance of systemic lupus erythematosus (80.60%)

in the study population restricts the representativeness of other systemic diseases, such as vasculitides and connective tissue disorders. Consequently, the overall conclusions are largely driven by lupus nephritis data, with limited extrapolation to less frequent conditions.

Third, the exclusion of patients with diabetes mellitus and chronic systemic infectious diseases (HIV, hepatitis B and C, and malaria) may limit the generalizability of the findings, particularly in the Sub-Saharan African context, where these conditions represent a substantial burden of kidney disease.

Fourth, electron microscopy was not routinely available in our center and therefore could not be included in the diagnostic evaluation. This limitation may have affected the accuracy of classification of certain glomerular diseases, particularly early-stage lesions and subtle ultrastructural abnormalities.

Fifth, although immunofluorescence was performed when tissue was available, technical constraints occasionally limited its use, which may have influenced the precise characterization of immune deposits in some cases.

Finally, the absence of long-term clinical follow-up data prevented the assessment of renal outcomes and response to treatment, thereby limiting the prognostic interpretation of histopathological findings.

Data Availability

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Statement of Ethics

The authors declare that the work described was carried out in accordance with the World Medical Association's Code of Ethics (Declaration of Helsinki) applicable to studies involving human subjects.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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